

# Dynamics and analysis of chronic brucellosis in sheep

## Abstract

We proposed and studied a new fractional-order model for the transmission dynamics of brucellosis with a special focus on the sheep-to-sheep transmission. Two control strategies namely; culling and vaccination rate are incorporated in the model. We computed the basic reproduction number  $R_0$  and we studied the global stability of disease-free and endemic equilibrium point in terms of basic reproduction number  $R_0$ : We found that both the disease-free and endemic equilibrium points are globally stable whenever  $R_0 < 1$  and  $R_0 > 1$  respectively. In numerical simulations, we performed the sensitivity analysis of the model and expressed the relationship between model parameters and  $R_0$ : We noted that, increase on the magnitude of model parameters with negative correlation coefficients would significantly reduce the spread of Brucellosis disease in the population. Moreover, model validation and parameter estimation for fractional-order and classical integer-order derivatives was carried out using real brucellosis data for Egypt, 1999-2011. Overall, we noted that fractional-order model gave better prediction of brucellosis compared to classical integer-order model. Furthermore, we investigated the role of memory effects on the transmission of brucellosis in the population. We observe that, the memory effects have influence on the transmission of brucellosis in the community. In addition, we noted that the aforementioned control strategies have the potential to reduce the transmission of brucellosis in

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the population. In particular, we observed that whenever the culling and vaccination rate is greater than 40% and 50% respectively, the disease dies out in the population.

Keywords: Brucellosis, Fractional-order model, Global stability, Sensitivity analysis, parameter estimation.

## 1 Introduction

Globally, human brucellosis remains an important and widespread infection [1]. *Brucella melitensis* is responsible for the vast majority of human cases [2]. Sheep and goats represent the natural hosts of *B. melitensis* [3, 4]. Domesticated species such as cattle, sheep, horse and goats are regarded as the main source of human brucellosis [5], in which transmission may occur directly or through the consumption of unpasteurised dairy products [6]. Brucellosis is transmitted to humans mainly by direct contact with animals or by consumption of milk products [7]. Although the disease is well contained in Australia and the UK, the annual global incidence of brucellosis is estimated above 500 000 [8, 9]. Brucellosis is endemic in Mediterranean areas, the south and the center of America, Africa, Asia, Arab peninsula, Indian subcontinent and the Middle East [5]. In animals, brucellosis is transmitted by direct contact transmission through the brucella carriers or indirect contact transmission when animals ingest contaminated forages or the excrement containing large quantities of bacteria, generally discharged by infected animals [6].

Since human-to-human transmission of the disease is rare the ultimate management of human brucellosis can be achieved through effective control of brucellosis in animal population. In addition the number one Sustainable Development Goal concerns ending poverty. Household income is identified as the major way by which extreme poverty can be reduced in developing countries. As a result, stakeholders and policy makers have turned their focus on livestock production as a means of raising income and improving the livelihood of rural dwellers. The livestock industry does not only supply manure for crop and vegetable growers but it also ensures the sustainability of food and nutrients and financial security, all of which contribute to raise the standard of living, particularly in rural areas.

Mathematical models have proved to be essential guiding tools for epidemiologists, biologists as well as policy makers (See for example [10, 11, 12, 13, 14, 15, 16, 17, 18]). Re-

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cently, modelling the transmission dynamics of brucellosis, is one of the most common global zoonoses [19], has been an interesting topic for a number of researchers (see, for example [6, 20, 21, 23, 24, 25, 26, 27, 28, 29]). It is undeniable that these studies and several other have produced several useful results and significantly improved the existing knowledge on brucellosis dynamics. Understanding the role of memory effects on short and long-term dynamics of infectious diseases is one of the emerging areas in the biological research. Thus, in this study a mathematical model for brucellosis based on Fractional Calculus (FC) is proposed and analyzed. Although this study is not the first to incorporate FC in studying brucellosis transmission (see, for example [30]) the proposed model is unique from those in literature. Although the fractional derivative has several definitions such as those derived from Riemann-Liouville, Caputo, Liouville, Weyl, Riesz, Grunwald-Litnikov, Marchaud and Hier, Caputo-Fabrizio-Caputo, Atanga-Baleanu, Atanga-beta derivative, M-fractional derivative, Atangana-Koca, conformable derivative, Atanga-Gomez, Variable-order and fractal-fractional idea [31, 32], the model proposed in this study will be based on the Caputo derivative. The rationale of choosing the Caputo derivative is that the Caputo derivative for a given function which is constant is zero. Thus, the Caputo operator computes an ordinary differential equation, followed by a fractional integral to obtain the desired order of fractional derivative [30, 33, 34, 35]. Most importantly, the Caputo fractional derivative allows the use of local initial conditions to be included in the derivation of the model [30, 33, 34, 35].

To the best of our knowledge, none of the models proposed as of to date has incorporated the aspect of chronic animals. According to Evermann and Eriks [36], brucellosis ecology can be segmented as infection rate, attack rate (progression to clinical disease) and mortality/morbidity (chronic carrier state). Most common clinical signs of brucellosis infection in sheep are abortions, stillbirths and the birth of weak offspring. A given number of animals born from brucella infected females may be latent carriers (approximately 5%) and can only be identified by immunological tests after their first or second pregnancy [37, 38]. However, according to some researchers animals infected with brucellosis generally abort only once [39], and clearly if the animal is not detected at this stage it will become chronic. Undoubtedly, effective management of brucellosis can be attained if emphasis is placed on multidisciplinary research aimed at addressing the underlying relationship between the disease ecology and prevalence.

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The remainder of this paper is organized as follows. In Section 2, we present preliminaries on the Caputo fractional calculus. Followed by the proposed model and analytical results in Section 3. In Section 4, numerical simulations are done in order to verify theoretical results presented in the study. Finally, we conclude the paper with a concluding remark in Section 5.

## 2 Preliminaries on the Caputo fractional calculus

We begin by introducing the definition of Caputo fractional derivative and state related theorems (see, [40]) that we will utilise to derive important results in this work.

Definition 1. Suppose that  $\alpha > 0$ ;  $t > b$ ;  $a, b; t \in \mathbb{R}$ : The Caputo fractional derivative is given by

$D_{a+}^{\alpha} f(t)$

$= \int_a^t f^{(n)}(\tau) d_{\tau}^{n-\alpha}$

$n-1 < \alpha < n$ ;  $n \in \mathbb{N}$ : (1)

$f^{(n)}(\tau)$

$n-1 < \alpha < n$ ;  $n \in \mathbb{N}$ : (1)

Definition 2. (Linearity property [40]). Let  $f(t); g(t) : [0; b] \rightarrow \mathbb{R}$  be such that

$D_{a+}^{\alpha}$

$f(t)$  and

$g(t)$  exist almost everywhere and let  $c_1, c_2 \in \mathbb{R}$ : Then,

$D_{cb}^-$

$D_{cb}^- (c_1 f(t) + c_2 g(t))$  exists

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$D_{cb}^- (c_1 f(t) + c_2 g(t)) = c_1$

$D_{cb}^-$

$D_{cb}^- (c_1 f(t) + c_2 g(t))$  exists

everywhere, and

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$D_{cb}^- (c_1 f(t) + c_2 g(t)) = c_1$

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Definition 3. (Caputo derivative of a constant [34]). The fractional derivative for a constant function  $f(t) = a$  is zero, that is,

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$D_{cb}^- a = 0$ : (3)

Let us consider the following general type of fractional differential equations involving Caputo derivative:

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$D_{cb}^-$

$D_{cb}^- x(t) = f(t; x(t))$ ;  $t \in (0, 1)$ ; (4)

with initial condition  $x_0 = x(b)$ :

Theorem 2.1. (Uniform Asymptotic Stability [40, 41]). Let  $x_*$  be an equilibrium point for the non-autonomous fractional order system (4) and  $\Omega \subset \mathbb{R}^n$  be a domain containing  $x_*$ : Let

$L : [0;1] \times \mathbb{R} \rightarrow \mathbb{R}$  be a continuously differentiable function such that

$M_1(x) \leq N(t; x(t)) \leq M_2(x)$

and

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### 3 Model Formulation and Analytical Results

The total animal population  $N(t)$  at time  $t$  is subdivided into compartments of: susceptible  $S(t)$ , vaccinated  $H(t)$ , exposed  $E(t)$ , clinically infected  $I(t)$ , and chronic carrier state  $L(t)$ .

Thus,  $N(t) = S(t) + H(t) + E(t) + I(t) + L(t)$ : Susceptible animals are exposed to the disease through direct contact with exposed, clinically infected and chronic animals. Although, brucellosis can be transmitted indirectly through environment, prior studies [20, 21] suggest that form of transmission plays a relatively small role on the spread of brucellosis, and as such we have ignored this concern in our study.

Here, brucellosis transmission rate is being modeled by the mass action incidence since it is appropriate when  $N(t)$  is not too large [22]. We assume that the transmission rate is dependent on the size of the population which implies that the contact rate is an increasing

function of the population. The mass action incidence is density- dependent since contact rate per infective is proportional to the density of the infectious host.

The model ow chart and corresponding fractional-order equations for brucellosis dynamics are given below:

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Figure 1: The model ow chart of brucellosis transmission

$${}_{cb}D_{\tau} S(t) = \lambda - \beta_1(E(t) + I(t) + L(t))S(t) - \beta_2 H(t) S(t) - (\mu + \nu)S(t);$$

$${}_{cb}D_{\tau} H(t) = \beta_1 S(t) - (\mu + \nu)H(t) - \delta H(t);$$

$${}_{cb}D_{\tau} E(t) = \beta_2 S(t) - (\mu + \nu)E(t) - \delta E(t);$$

$${}_{cb}D_{\tau} I(t) = \delta E(t) - (\mu + \nu + d + c)I(t);$$

$${}_{cb}D_{\tau} L(t) = \nu I(t) - (\mu + d)L(t);$$

9>>>>>>>>>>=

>>>>>>>>>>;

(5)

where  $cb$

$D_{\tau}$

$\tau$  denotes the Caputo-fractional calculus and  $\alpha$  with  $0 < \alpha < 1$  is fractional order.

Furthermore the death rate is denoted by  $\mu$ , the parameter  $\lambda$  is the recruitment rate,  $d$  is the disease-related death rate,  $\nu$  is the vaccination rate,  $\delta$  is the immunity waning rate.

The mass action incidence is given by  $\beta_1 S(t)(E(t)+I(t)+L(t))$ , and  $\beta_2 H(t)(E(t)+I(t)+L(t))$

where  $\beta_1$  is the disease direct transmission rate such that  $\beta_1 N$  is the number of adequate contact required for the transmission of brucellosis,  $\beta_2$  is the modification factor,  $\nu$  is the incubation rate,  $c$  is the culling rate of symptomatic infectious animals, and  $\delta$  is the rate of progression to chronic state. All model parameter and variables are considered to be positive.

### 3.1 The Basic Reproduction Number and Existence of Equilibria

In this section, we study the basic reproduction number and the existence of a disease-free equilibrium and an endemic equilibrium of system (5). System (5) always has a disease-free equilibrium  $E_0 = (S_0; H_0; E_0; I_0; L_0) = (S_0; H_0; 0; 0; 0)$ , with  $S_0 = \frac{\lambda}{\mu + \nu}$

$\frac{\lambda}{\mu + \nu}$ ,  $H_0 =$

$\frac{\lambda}{\mu + \nu}$ ; and  $S_0 + H_0 = \frac{\lambda}{\mu + \nu}$

$\frac{\lambda}{\mu + \nu}$ : By means of the method of the next gener-

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ation matrix (see, for example, van den Driessche and Watmough [42] , one obtains the basic reproduction number of system (5) as follows:

$$R_0 = R_E + R_I + R_L$$

=

$$\frac{\lambda}{\mu + \nu} (S_0 + H_0)$$

$$(\mu + \nu)$$

+

$$\frac{\lambda}{\mu + \nu} (S_0 + H_0)$$

$$(\mu + \nu)(\mu + \nu + d + c)$$

$$+ \frac{\beta(S_0 + H_0)}{(\lambda + \mu)(\lambda + \mu + d + c)(\lambda + d)}$$

(6)

$R_0$  is the average number of secondary transmissions by a single infectious individual in a fully susceptible population,

where

$$R_E = \frac{\beta(S_0 + H_0)}{(\lambda + \mu)}$$

; accounts for the average number of new infections generated by exposed animals;

$$R_I = \frac{\beta(S_0 + H_0)}{(\lambda + \mu)(\lambda + \mu + d + c)}$$

; gives the number of new infections generated by infectious animals; and;

$$R_L = \frac{\beta(S_0 + H_0)}{(\lambda + \mu)(\lambda + \mu + d + c)(\lambda + d)}$$

; measures the average number of secondary brucellosis infections generated by chronically infected animals.

In addition to the disease-free equilibrium  $E_0$ , system (5) has a unique endemic equilibrium  $E_* = (S_*; H_*; E_*; I_*; L_*)$ , where from the last two equations in (5) we have,

$$I_* = \frac{E_*}{(\lambda + \mu + d + c)}$$

;  $L_* =$

$$\frac{E_*}{(\lambda + \mu + d + c)(\lambda + d)}$$

; and  $(E_* + I_* + L_*) = ME_*$  (7);

with

$$M = \frac{(\lambda + d)(\lambda + \mu + d + c) + \mu(\lambda + \mu + d)}{(\lambda + d)(\lambda + \mu + d + c)}$$

(8)

the first two equations in (5) lead to

$$S_* = \frac{\mu(\lambda + \mu + ME_*)}{(\lambda + \mu + ME_*)(\lambda + \mu + ME_*) - \mu^2}; ; \text{ and}$$

$$H_* =$$

$$\frac{\mu^2}{(\lambda + \mu + ME_*)(\lambda + \mu + ME_*) - \mu^2}; (9)$$

for  $E_* = 0$ , substituting the third equation in (7) into the third equation in (5) yields,

$$(S_* + H_*) =$$

$$\frac{\mu}{M}$$

: (10)

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Substituting (9) into (10) gives:

$$F(E_*) =$$

$$\frac{(\lambda + \mu + \beta E_0)}{(\lambda + \mu + \beta E_0)(\lambda + \mu + \beta E_0) - \beta M} < 1$$

$$\frac{(\lambda + \mu)}{\beta M} > 1 \quad (11)$$

Direct calculation for  $E_0 = 0$  shows:

$$D_t F(E_0) = \beta M [(\lambda + \mu + \beta E_0)^2 + 2(\lambda + \mu + \beta E_0) + a] < 0 \quad (12)$$

Where

$$a = (\lambda + \mu)^2 + 2\lambda\mu + (\lambda + \mu)^2 + 2\lambda\mu + 2\lambda\mu + (\lambda + \mu)^2; \quad (13)$$

then the function  $F(E_0)$  is monotonic decreasing for  $E_0 > 0$ , then we can define the function

$$F(0) = \frac{(\lambda + \mu + \beta E_0)}{(\lambda + \mu + \beta E_0) - \beta M} > 1 \quad (R_0 > 1); \quad (14)$$

Therefore, by monotonicity of a function  $F(E_0)$  there exists a unique positive root in the interval  $(0; 1)$  when  $R_0 > 1$  and there is no positive root in the interval  $(0; 1)$  when  $R_0 < 1$ .

Thus model (5) has a unique endemic equilibrium  $E_0 = (S_0; H_0; E_0; I_0; L_0)$ .

### 3.2 Global Stability

In this section, we are concern with the global stability of the disease-free equilibrium  $E_0$  and the endemic equilibrium  $E_0$  of system (5).

Theorem 3.1. If  $R_0 < 1$ , then the disease-free equilibrium  $E_0$  is globally asymptotically stable.

Proof. Consider the following Lyapunov function:

$$V(t) =$$

$$\frac{(\lambda + \mu)}{\beta} + \frac{(\lambda + \mu + \beta E_0)}{(\lambda + \mu + \beta E_0)(\lambda + \mu + \beta E_0) - \beta M} > 1$$

$$E(t) \quad (15)$$

$$\frac{(\lambda + \mu + \beta E_0)}{(\lambda + \mu + \beta E_0)(\lambda + \mu + \beta E_0) - \beta M} > 1$$

$$I(t) +$$

$$\frac{(\lambda + \mu + \beta E_0)}{(\lambda + \mu + \beta E_0)(\lambda + \mu + \beta E_0) - \beta M} > 1$$

$$L(t):$$

Then the fractional time derivative of  $V(t)$  along the solutions of model (5) yields :

$${}^{cb}D_{t_0}^{\alpha} V(t) =$$

$$\frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dV(s)}{ds} ds + \frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dV(s)}{ds} ds + \frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dV(s)}{ds} ds$$

$${}^{cb}D_{t_0}^{\alpha} E(t) \quad (16)$$

$$\frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dE(s)}{ds} ds + \frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dE(s)}{ds} ds$$

$${}^{cb}D_{t_0}^{\alpha} I(t) +$$

$$\frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dI(s)}{ds} ds$$

$${}^{cb}D_{t_0}^{\alpha} L(t):$$

$$= \frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dL(s)}{ds} ds$$

$$\frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dS(s)}{ds} ds + \frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{dH(s)}{ds} ds$$

$$S(t) + H(t)$$

$$\square 1$$

#

"

$$E(t) + I(t) + L(t)$$

#

:(17)

Since  $S(t) \geq S_0; H(t) \geq H_0;$

$$S_0 + H_0 = \frac{1}{\Gamma(\alpha)} \int_{t_0}^t \frac{d(S+H)}{ds} ds$$

for  $t \geq 0$  we have:

cb

$$D_t V(t) = -$$

$$\frac{1}{(S_0 + I_0)} + \frac{1}{(S_0 + I_0 + d_0)} \frac{1}{(S_0 + I_0 + d_0 + c_0)}$$

$$\frac{1}{(S_0 + I_0 + L_0)}$$

$$\square 1$$

$$\#$$

$$E(t) + I(t) + L(t)$$

$$\#$$

$$\vdots$$

$$=$$

$$R_0 \square 1$$

$$\#$$

$$E(t) + I(t) + L(t)$$

$$\#$$

$$(18)$$

Therefore,  $c_b$

$D_t V(t) < 0$  holds if  $R_0 < 1$ . Furthermore,  $c_b$

$D_t V(t) = 0$  if  $R_0 = 1$ . Thus, the largest invariant set of  $c_b$

$D_t V(t)$  is a singleton such that  $S(t) = S_0, H(t) = H_0, E(t) = I(t) = L(t) = 0$ : Therefore, from the LaSalle's invariance principle [43] the disease-free equilibrium of model (5) denoted by  $E_0$  is globally asymptotically stable whenever  $R_0 \leq 1$ . This completes the proof.

Next, we investigate the global stability of the endemic equilibrium point  $E_*$  of model (5) when  $R_0 > 1$ :

Theorem 3.2. If  $R_0 > 1$ , then model (5) has a globally asymptotically stable endemic equilibrium point.

Proof. In order to analyze the global asymptotic stability of the endemic equilibrium of model (5) we set:

$$x = S$$

$$S_*, y = H$$

$$H_*, z = E$$

$$E_*, u = I$$

$L_1$ , and  $v =$

$L_1$

$L_1$

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Thus, model (5) is transformed into the following form:

cb

$D_1$

$\dot{x}(t) = x$

—

$S_1$

—

1

x

□ 1

—

□  $E_1(z \square 1) \square I_1(u \square 1) \square L_1(v \square 1)$

—

+x

—

$H_1$

$S_1$

ny

x

□ 1

$o_1$

;

cb

$D_1$

$\dot{y}(t) = y$

—

$S_1$

$H_1$

—

x

y

□ 1

—

□  $E_1(z \square 1) \square I_1(u \square 1) \square L_1(v \square 1)$

—

;

cb

$D_1$

$\dot{z}(t) = z$

—

$S_1$

$E_1$

nxu

z

□ 1

o

+



Consider the Lyapunov function

$$W = S_1$$

$$+ (x - 1) \ln x$$

$$+ H_1$$

$$+ (y - 1) \ln y$$

$$+ E_1$$

$$+ (z - 1) \ln z$$

+

$$\frac{1}{2} (S_1 + H_1)(I_1 + L_1)$$

$$+ E_1 I_1$$

$$+ (u - 1) \ln u$$

+

$$\frac{1}{2} (S_1 + H_1) L_1$$

$$+ I_1 L_1$$

$$+ (v - 1) \ln v$$

:(20)

10

Differentiating  $W$  with respect to  $t$  along solutions of (19) yields:

$\frac{d}{dt}$

$$W(t) = (x - 1)$$

-

-

1

x

$$- 1$$

$$- \frac{1}{2} E_1 S_1 (z - 1) - \frac{1}{2} I_1 S_1 (u - 1) - \frac{1}{2} L_1 S_1 (v - 1)$$

$$+ (x - 1)$$

n

$$- \frac{1}{2} H_1 S_1$$

$$+ \frac{1}{2} n y$$

x

$$- 1$$

oo

$$+ (y - 1)$$

$$- S_1$$

-

$x$   
 $y$   
 $\square 1$   
 $\bar{\square} \_E_H(z \square 1) \square \_I_H(u \square 1) \square \_L_H(v \square 1)$   
 $\bar{\square} + (z \square 1)$   
 $n$   
 $\_S_I$   
 $nxu$   
 $z$   
 $\square 1$   
 $o$   
 $+ \_H_I$   
 $nyu$   
 $z$   
 $\square 1$   
 $o$   
 $+ \_S_L$   
 $nxv$   
 $z$   
 $\square 1$   
 $oo$   
 $+ (z \square 1)$   
 $n$   
 $\_H_L$   
 $nyv$   
 $z$   
 $\square 1$   
 $o$   
 $+ \_S_E_{fx} \square 1g + \_H_E_{fy} \square 1g$   
 $o$   
 $+$   
 $\_ (S_ + H_)(I_ + L_)$   
 $\_E_ (u \square 1)$   
 $n$   
 $\_E_$   
 $nz$   
 $u$   
 $\square 1$   
 $oo$   
 $+$   
 $\_ (S_ + H_)L_$   
 $\_I_ (v \square 1)$   
 $n$   
 $\_I_$   
 $nu$   
 $v$   
 $\square 1$   
 $oo$   
 $= F(x; y; z; u; v):$



y

-  
+ \_I\_S\_

-  
3 □

1

x

□

z

u

□

xu

z

-  
+ \_S\_L\_

-  
4 □

1

x

□

z

u

□

u

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xv

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-  
+ \_H\_I\_

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4 □

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+ \_H\_L\_

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5 □

1

x

□

$x$   
 $y$   
 $z$   
 $u$   
 $v$   
 $o$

$$= F(x; y; z; u; v): (23)$$

Since the arithmetic mean is greater or equal to the geometric mean, i.e

$D_{t^{\alpha}}$

$$W(t) =$$

$F(x; y; z; u; v) \geq 0$ , it can easily be verified that

$D_{t^{\alpha}}$

$$W(t) \geq 0 \text{ provided that } S_0, H_0, E_0, I_0, L_0$$

are positive, where the equality

$D_{t^{\alpha}}$

$W(t) = 0$  holds only for  $x = y = z = u = v = 1$ . Therefore

$D_{t^{\alpha}}$

$D_{t^{\alpha}}$

$W(t) \geq 0$  holds. Then the endemic equilibrium point  $E_0$  is globally asymptotically stable if  $R_0 > 1$  by LaSalle's invariance principle [43].

## 4 Numerical Simulations and Discussion

In this section, we utilize the MATLAB programming language to numerically solve the model system (5) and assess the behavior of solution for fractional-order derivatives. We perform the fractional Adam-Bashforth-Moulton scheme to simulate the model (5) as illustrated below;

Consider the nonlinear differential equation:

$D_{t^{\alpha}}$

$D_{t^{\alpha}}$

$$x'(t) = f(t; x(t)); 0 \leq t \leq T; (24)$$

with the following initial conditions:

$$x_p(t) = x_p$$

$$0; p = 0; 1; 2; \dots; n-1: (25)$$

Now, with operating by the fractional integral operator on the equation (24), we can obtain on the solution  $x(t)$  by solving the following equation:

$$x(t) =$$

$$\int_0^t X_j d\tau$$

$$p=0$$

$$x_p$$

$$p!$$

$$t^p +$$

$$1$$

$$\int_0^t$$

$$Z t$$

$$0$$

$$(t - \tau)^{p-1} f(\tau; x(\tau)) d\tau: (26)$$

Diethelm [47] applied the predictor-corrector scheme based on the Adam-Bashforth-Moulton algorithm to establish the solution for equation (24). Setting  $h = \tau$

$N$ ,  $t_n = nh$  and  $n = 0; 1; 2; \dots; N \in \mathbb{Z}^+$ . Therefore we discretized equation (24) as follows:

$$h(t_{n+1}) = \sum_{j=0}^{n+1} X_j \frac{h^j}{j!} + \sum_{m=0}^{n+1} a_{m;n+1} f(t_m; \underline{v}_{n+1}) \quad (27)$$

where

$$a_{m;n+1} = \begin{cases} (n+1 - m) \binom{n+1}{m} h^m; & m = 0; \\ \binom{n+1}{m} h^m; & 1 \leq m \leq n; \\ 1; & \text{if } m = n+1; \end{cases}$$

and the predicted value  $\underline{v}_{n+1}$  is determined by

$$h(t_{n+1}) = \sum_{j=0}^{n+1} X_j \frac{h^j}{j!} + \sum_{m=0}^{n+1} b_{m;n+1} f(t_m; h(t_m)); \quad (28)$$

where

$$b_{m;n+1} = \frac{h^m}{((n+1-m)! (n-m)!)}; \quad (29)$$

The error estimate is

$$\max_{0 \leq m \leq k} |j_m(t_m) - h(t_m)| = O(h^v); \quad (30)$$

with  $k \in \mathbb{Z}^+$  and  $v = \min(2, 1 + \underline{v})$ .

#### 4.1 Application of Adam-Bashforth-Moulton Scheme to the proposed model

In this section, we solved numerically the nonlinear fractional-order model (5) by Adam-Bashforth-Moulton method. In the view to the generalized Adam-Bashforth-Moulton method, the proposed scheme for the model system (5) has the following form:

$$S(t_{n+1}) = S_0 +$$

$h_n$

$$\sum_{m=0}^n a_{m;n+1} f_S$$

$f_S$

$\sum_{m=0}^n$

$$t_m; S(t_m); H(t_m); E(t_m); I(t_m);$$

$$L(t_m)$$

—

$+ h_n$

$$\sum_{m=0}^n a_{m;n+1}$$

$P_n$

$$m=0 a_{m;n+1} f_S$$

$\sum_{m=0}^n$

$$t_m; S(t_m); H(t_m); E(t_m); I(t_m);$$

$$L(t_m)$$

—

;

$$H(t_{n+1}) = H_0 +$$

$h_n$

$$\sum_{m=0}^n a_{m;n+1}$$

$f_H$

$\sum_{m=0}^n$

$$t_m; S(t_m); H(t_m); E(t_m); I(t_m);$$

$$L(t_m)$$

—

$+ h_n$

$$\sum_{m=0}^n a_{m;n+1}$$

$P_n$

$$m=0 a_{m;n+1} f_H$$

$\sum_{m=0}^n$

$$t_m; S(t_m); H(t_m); E(t_m); I(t_m);$$

$$L(t_m)$$

—

;

$$E(t_{n+1}) = E_0 +$$

$h_n$

$$\sum_{m=0}^n a_{m;n+1}$$

$f_E$

$\sum_{m=0}^n$

$$t_m; S(t_m); H(t_m); E(t_m); I(t_m);$$

$$L(t_m)$$

—

$+ h_n$

$$\sum_{m=0}^n a_{m;n+1}$$

$P_n$

$$m=0 a_{m;n+1} f_E$$







(b)

Figure 2: The model system (5) fitted to brucellosis cases from Egypt as reported in [44] at  $\alpha = 0.826$ . The red circles denote the real data and the smooth line denotes the model prediction to the real data.

Figure (2) shows commutative detected cases of brucellosis as reported in Egypt. We used the 13 yearly reports cases to fit in the model system (5). The prediction ability between fractional order model and the classical model is investigated. Overall we observed that the estimates for 17

the fractional order model are close to the real data for the entire period of 13 years compared to the estimates of the classical integer model. Therefore we conclude that the fractional order model has better forecasts compared to the classical integer model.

(a)

Figure 3: The model system (5) shows the residuals against the time series for brucellosis cases

from Egypt as reported in [44]

Figure (3) shows the graphical representation of residuals for the model system (5) of brucellosis

cases reported in [44]. Overall, one can note that the residuals did not follow any particular path (exhibited random pattern) which shows that the model (5) present better forecasts to the reported real data in [44].

#### 4.3 Sensitivity analysis of the reproduction number

In this section we perform the sensitivity analysis and investigate what happens to some dependent variables when either one or more its independent variables are altered. To identify the parameters that are strongly correlated positively or negatively to  $R_0$ ; we conducted global sensitivity analysis of the model system (5) using partial rank correlated coefficient developed in [45] and the values of the parameters used in the model simulations are in table (2).

Definition 4. (See, [45]) The normalized sensitivity index of  $R_0$  which depends on differentiability of parameter,  $\theta$  is defined as follows:

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$\frac{\partial R_0}{\partial \theta}$

$=$

$\frac{\theta}{R_0}$

$\frac{\partial R_0}{\partial \theta}$

$=$

$\frac{\theta}{R_0}$

$\frac{\partial R_0}{\partial \theta}$

(38)

The implication of the sensitivity analysis is that the model parameters whose sensitivity index is positive increase the magnitude of  $R_0$  whenever they are increased and those with a negative index decrease the  $R_0$  whenever they are increased. From (38), the value of normalized

sensitivity index for each parameter used in the model (5) is summarized in table (3):

Table 2: Definition of Parameters and values

Symbol	Definition	Value	Units	Source
$\lambda$	Recruitment rate	11,629,200	year <sup>-1</sup>	[21]
$\mu$	Natural elimination rate	0.25	year <sup>-1</sup>	[21]
$\omega$	Vaccination waning rate	0.4	year <sup>-1</sup>	[21]
$\beta$	Modification factor	0.18	unitless	[21]
$\nu$	Vaccination rate	0.316	year <sup>-1</sup>	[21]
$\tau$	Incubation rate	3.4	year <sup>-1</sup>	[23]
$\gamma$	Culling rate	0.15	year <sup>-1</sup>	[21]

d Disease mortality rate  $\square$  year $\square$ 1\_tted  
 \_ Sheep -to-sheep transmission rate  $\square$  year $\square$ 1\_tted  
 \_ Rate of progression to chronic state  $\square$  year $\square$ 1\_tted

Table 3: Sensitivity analysis of parameters for the model system (5)

Parameter	__	__	__	__	c		
Index	+1.0000	-1.0000	+0.2955	+0.2565	-0.2955	-0.4200	$\square$ 0:4942
Parameter d	__	__					
Index	-0.5351	+1.0000	+0.4493				

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Figure 4: Sensitivity analysis of the model system (5)

From the results in Fig. 4, model parameters with positively partial rank correlation coefficient to  $R_0$ ; that is., whenever they are increased  $R_0$  increases and those with negatively correlated to  $R_0$ ; whenever they increased  $R_0$  decreases. Overall, we can note that parameters \_\_, \_\_; and \_\_ have high influence on the magnitude of  $R_0$ . For example, an increase in \_\_ by 20% will lead to an increase in the magnitude of  $R_0$  by 20%. On the other-hand, parameters \_\_, \_\_; \_\_, c, and d whenever they increase the magnitude of  $R_0$  decreases. Therefore, to reduce the spread of brucellosis in animal population the policy markers should target the mitigation that increase the parameters with negative and decrease the parameters with positively correlated to  $R_0$ . In particular, we one can note that increasing the vaccination rate (modeled by parameter, \_\_) and culling rate (modeled by parameter, c) will reduce the spread of brucellosis in animal population.

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(a) (b)

Figure 5: Effects of varying (a) culling rate c on  $R_0$  (b) vaccination rate \_\_ on  $R_0$

Numerical results in Fig. 5 (a) culling rate (modeled by parameter c) on  $R_0$ . From the results we observed that increasing the culling rate on infected sheep decrease the magnitude of  $R_0$ . We observed that, whenever c is greater than 0:4 the disease dies in the population. Figure 5 (b), we investigated the effect of vaccination modeled by parameter \_\_ on  $R_0$ . We noted that whenever the \_\_ is greater than 0:5 the disease dies in the community.

(a) (b)

Figure 6: Effects of varying (a) vaccination waning rate (modeled by parameter \_\_) on  $R_0$  (b) rate of progression to chronic stage (modeled by parameter \_\_) on  $R_0$

Numerical results in Fig. 6 (a) we assessed the effects of vaccination waning rate modeled by parameter \_\_ on  $R_0$ . From the results we noted that increasing the vaccination waning rate of vaccinated sheep increases the magnitude of  $R_0$ . In particular, whenever \_\_ is greater than

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0:5 the disease persists in the population. Figure 6 (b), we investigated the effects of rate of progression to chronic stage modeled by parameter \_\_ on  $R_0$ . We observed that whenever the \_\_ is greater than 0:5 the disease persists in the community.

Figure 7: Contour plot of  $R_0$  as the function of culling rate c and vaccination rate \_\_. We simulated the model (5) at \_\_ = 0:015; d = 0:00055; and \_\_ = 8:444  $\square$  10 $\square$ 6

Figure (7) shows the contour plot of  $R_0$  as the function of culling rate c and vaccination rate \_\_. The results showed that, increase of culling rate on asymptomatic sheep the value of  $R_0$  decreases. In particular, we noted that whenever the culling rate is greater than 0:4 the disease dies out in the population.

Figure 8: Contour plot of  $R_0$  as the function of culling rate c and modification factor on the disease transmission modeled by parameter . We simulated the model (5) at \_\_ = 0:015; d = 0:00055; and \_\_ = 8:444  $\square$  10 $\square$ 6

Figure (7) shows the contour plot of  $R_0$  as the of culling rate c and modification factor on the

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disease transmission modeled by parameter . Overall, we observed that increase of culling

rate and modification factor decrease the magnitude of  $R_0$ . One can note that whenever the culling rate is greater than 4% the magnitude of  $R_0$  is less than unity.

Figure 9: Mesh plot of  $R_0$  as the function of culling rate  $c$  and vaccination rate  $\omega$ . We simulated the model (5) at  $\alpha = 0.015$ ;  $d = 0.00055$ ; and  $\beta = 8.444 \times 10^{-6}$

Figure (9) shows the mesh plot of  $R_0$  as the function of culling rate (modeled by parameter  $c$ ) and vaccination rate (modeled by parameter  $\omega$ ). Overall, we noted that increase on culling and vaccination rate decreases the magnitude of  $R_0$ : Therefore, we can conclude that both culling and vaccination rate have the potential to minimize the spread of disease in the population.

#### 4.4 Simulation of the model to support the analytical results

In this section, we solve the model system (5) numerically at  $\alpha \in (0; 1]$  to support the analytical results. We first perform the numerical results at  $R_0 < 1$ , followed by simulation at  $R_0 > 1$  to show the behavior of dynamical solution of the model (5).

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(a) (b)

(c) (d)

Figure 10: Dynamical solutions of model system (5) at  $R_0 < 1$  with different order derivatives,  $\alpha = 0.6; 0.7; 0.8; 1$ , leading to  $R_0 \in [0.0142; 1)$ .

Numerical simulation in Fig. (10) shows the convergence of model solutions to the disease-free equilibrium with different fractional order derivatives. The solution were obtained upon setting  $d = 1.5 \times 10^{-6}$ ;  $\beta = 8.944 \times 10^{-9}$ ; and  $\omega = 1.5 \times 10^{-5}$ ; giving  $R_0 \in [0.0142; 1)$ .

Overall, we observed that as the order of derivatives decrease from unity the value of the reproduction number  $R_0$  decreases close to 0 and the time taken by the solution to converge to the disease-free equilibrium decreases.

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(a) (b)

(c) (d)

Figure 11: Dynamical solutions of model system (5) at  $R_0 > 1$  with different order derivatives,  $\alpha = 0.6; 0.7; 0.8; 1$ , leading to  $R_0 \in (1; 9.6235]$ .

Numerical simulation in Fig. (11) shows the convergence of model solutions to the endemic equilibrium with different fractional order derivatives. The solution were obtained upon setting  $d = 0.015$ ;  $\beta = 8.944 \times 10^{-6}$ ; and  $\omega = 1.5 \times 10^{-4}$ ; giving  $R_0 \in (1; 9.6235]$ . Overall, we observed that whenever the derivative order  $\alpha$  approaches 1, the value of the reproduction number  $R_0$  increases and the memories of biological species decreases as a result the number of infections increase over time. Additionally, one can note that as the order of derivatives decrease from 1 the time taken by the solution to attain its stability decreases.

## 5 Concluding Remarks

Brucellosis is one of the zoonotic diseases caused by bacteria belonging to the genus *Brucella*. This bacteria can cause infections to both wild and domestic animals such as cattle, goats, sheep, dogs, wild hogs and etc. Recently, mathematical modeling of infectious disease using

fractional order derivatives are suggested in the literature [34, 40, 41]. It is worth noting that fractional order models can properly capture the memory effects and hereditary properties of biological systems. Therefore, in this study we analyzed the Caputo derivative non-integer order Brucellosis model. We quantitatively studied the model and provided its analysis in details. We investigated the global stability of both disease-free and endemic equilibrium points of non-integer Brucellosis model using well constructed Lyapunov functions. We found that the disease free and endemic equilibrium point is global stable whenever  $R_0 < 1$  and  $R_0 > 1$  respectively. In numerical simulations, first of all we qualitatively performed global sensitivity analysis of the model and expressed the relationship between  $R_0$  and the model parameters. Overall, we noted that for the disease management increase in magnitude of

the parameters with negative correlation coefficients would significantly reduce the spread of Brucellosis disease in the population.

Extensive investigation of the relationship between  $R_0$  and control strategies namely; culling rate (modeled by parameter  $c$ ) and vaccination rate (modeled by parameter  $v$ ) have been investigated. The results revealed that both culling and vaccination rate have the nonlinear relationship with  $R_0$ : In particular, we noted that whenever the culling and vaccination rate is greater than 40% and 50% respectively, the disease dies out in the population. Parameter estimation was carried out using the nonlinear least square method which produced best fitted values of  $d$ ;  $v$  and  $c$ : Model validation was carried out using the estimated parameters and the results was compared with both classical integer and fractional order model. Overall, we noted that fractional order model gave better prediction of Brucellosis disease compared to integer order derivative. Furthermore, we investigated the role of memory effects on the transmission dynamics of the Brucellosis by varying the order of derivatives  $\alpha$ : We observed that the memory of biological species have influence on the dynamics of Brucellosis disease transmission. In particular, one can note that as the order of derivatives decrease from 1, the number of infections generated in the population decrease and thus the disease dies in the community.

#### Availability of Data

All data have been included in the manuscript.

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#### Competing Interest

The authors declare that they have no conflicts of interest.

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#### Authors Contributions

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